



Food and Drug Administration
10903 New Hampshire Avenue
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April 3, 2015

BIO-RAD LABORATORIES, INC.
JACKIE BUCKLEY
REGULATORY AFFAIRS REP IV
4000 ALFRED NOBEL DR.
HERCULES CA 94547

Re: K142448

Trade/Device Name: VARIANT™ II TURBO HbA1c Kit – 2.0
Hemoglobin Capillary Collection System

Regulation Number: 21 CFR 862.1373

Regulation Name: Glycosylated hemoglobin assay

Regulatory Class: II

Product Code: PDJ, JKA

Dated: March 24, 2015

Received: March 24, 2015

Dear Ms. Jackie Buckley:

This letter corrects our substantially equivalent letter of March 24, 2015.

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA).

You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21

CFR Part 807); labeling (21 CFR Parts 801 and 809]); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulation (21 CFR Part Parts 801 and 809]), please contact the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address <http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm>. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to <http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm> for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address <http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm>.

Sincerely yours,

Stayce Beck -S

For : Courtney H. Lias, Ph.D.
Director
Division of Chemistry and Toxicology Devices
Office of In Vitro Diagnostics
and Radiological Health
Center for Devices and Radiological Health

Enclosure

Indications for Use

510(k) Number (if known)

k142448

Device Name

VARIANT™ II TURBO HbA1c Kit- 2.0

Hemoglobin Capillary Collection System

Indications for Use (Describe)

The VARIANT™ II TURBO HbA1c Kit- 2.0 is intended for the quantitative determination of hemoglobin A1c (IFCC mmol/mol and NGSP %) in human whole blood using ion-exchange high-performance liquid chromatography (HPLC) on the VARIANT II TURBO Hemoglobin Testing System and VARIANT II TURBO Link Hemoglobin Testing System.

This test is to be used as an aid in diagnosis of diabetes and as an aid in identifying patients who may be at risk for developing diabetes.

The VARIANT II TURBO HbA1c Kit- 2.0 is intended for Professional Use Only.

The Hemoglobin Capillary Collection System (HCCS) is intended for the collection of human whole blood for the percent determination of hemoglobin A1c using Bio-Rad HPLC methods.

Type of Use (Select one or both, as applicable)

☒ Prescription Use (Part 21 CFR 801 Subpart D)

☐ Over-The-Counter Use (21 CFR 801 Subpart C)

PLEASE DO NOT WRITE BELOW THIS LINE – CONTINUE ON A SEPARATE PAGE IF NEEDED.

FOR FDA USE ONLY

Concurrence of Center for Devices and Radiological Health (CDRH) (Signature)

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510(k) Summary (Summary of Safety and Effectiveness)

This Summary of 510(k) Safety and Effectiveness is being submitted in accordance with the requirements of SMDA 1990 and 21 CFR 807.92.

The assigned 510(k) number is: _____.

Date Summary prepared: March 20, 2015

1. Applicant Name:

Bio-Rad Laboratories, Inc.
Clinical Diagnostics Group
4000 Alfred Nobel Drive
Hercules, California 94547

2. Contact Person:

Jackie Buckley
Telephone Number: (510) 741-5309
FAX: (510) 741-6471
E-Mail: Jackie_buckley@bio-rad.com

3. Device Name/Trade Name:

VARIANT™ II TURBO HbA1c Kit – 2.0
Classification Name: Hemoglobin A1c Test System
Common Name: HbA1c
Product Code: PDJ
C.F.R Section: 21 CFR 862.1373
Device classification: Class II

Hemoglobin Capillary Collection System
Classification Name: Tubes, Vials, Systems, Serum Separators, Blood Collection
Product Code: JKA
C.F.R Section: 21 CFR 862.1675
Device classification: Class II

4. Predicate Device:

COBAS INTEGRA 800 Tina-quant HBA1cDx Gen.2 assay (K121291)

5. Description of the Device:

The VARIANT™ II TURBO HbA1c Kit - 2.0 utilizes principles of ion-exchange high-performance liquid chromatography (HPLC). The samples are automatically diluted on the VARIANT™ II TURBO Sampling Station (VSS) and injected into the analytical cartridge. The VARIANT™ II TURBO Chromatographic Station (VCS) dual pumps deliver a programmed buffer gradient of increasing ionic strength to the cartridge, where the hemoglobins are separated based on their ionic interactions with the cartridge material. The separated hemoglobins then pass through the flow cell of the filter photometer, where changes in the absorbance at 415 nm are measured. An additional filter at 690 nm corrects for background absorbance.

The VARIANT™ II TURBO Clinical Data Management (CDM™) software performs reduction of raw data collected from each analysis. Two-level calibration is used for adjustment of the calculated HbA1c values. A sample report, including retention times of detected peaks and a chromatogram, is generated by the CDM for each sample. The A1c peak is shaded for ease of identification. The area is calculated using an exponentially modified Gaussian (EMG) algorithm and the result printed in either mmol/mol or % HbA1c format as selected by the user.

The VARIANT™ II TURBO HbA1c Kit – 2.0 is designed to be used on the standalone VARIANT™ II TURBO and the VARIANT™ II TURBO Link Hemoglobin Testing Systems. VARIANT™ II TURBO and the VARIANT™ II TURBO Link Hemoglobin Testing Systems are identical with respect to all operational and system components. Physically, the VARIANT™ II TURBO Link VSS outer case is modified for compatibility with a track system. Functionality of the VARIANT™ II TURBO Link has not changed, just the physical orientation to accommodate sample tube management on a track system.

6. Indications for Use:

The VARIANT™ II TURBO HbA1c Kit – 2.0 is intended for the quantitative determination of hemoglobin A1c (IFCC mmol/mol and NGSP %) in human whole blood using ion-exchange high-performance liquid chromatography (HPLC) on the VARIANT™ II TURBO Hemoglobin Testing System and VARIANT™ II TURBO Link Hemoglobin Testing System.

This test is to be used as an aid in diagnosis of diabetes and as an aid in identifying patients who may be at risk for developing diabetes.

The VARIANT™ II TURBO HbA1c Kit – 2.0 is intended for Professional Use Only.

The Hemoglobin Capillary Collection System (HCCS) is intended for the collection of human whole blood for the percent determination of hemoglobin A1c using Bio-Rad HPLC methods.

7. Substantial Equivalence Information:

Predicate Device Name:

Roche COBAS INTEGRA 800 Tina-quant HbA1c DX Gen. 2 assay

Predicate 510(k) number:

K121291

Table 1: Similarities with Predicate						
Feature	Candidate Device: VARIANT™ II TURBO HbA1c Kit – 2.0			Predicate Device: COBAS INTEGRA 800 HbA1c DX Gen. 2		Status
Intended Use	Intended for the quantitative determination of hemoglobin A1c (IFCC mmol/mol and NGSP %)			Intended for the quantitative determination of hemoglobin A1c (IFCC mmol/mol and NGSP %)		Same
Indications for Use - Diagnosis	This test is to be used as an aid in diagnosis of diabetes and as an aid in identifying patients who may be at risk for developing diabetes.			This test is to be used as an aid in diagnosis of diabetes and as an aid in identifying patients who may be at risk for developing diabetes.		Same
Indications for Use - Monitoring	Measurement of hemoglobin A1c is effective in monitoring long-term glycemic control in individuals with diabetes mellitus			Measurement of hemoglobin A1c is effective in monitoring long-term glycemic control in individuals with diabetes mellitus		Same
Specimen Type	Human Whole blood			Human Whole blood		Same
Matrices	K ₂ -EDTA, K ₃ -EDTA			K ₂ -EDTA, K ₃ -EDTA		Same
Measuring Interval	3.4 to 20.6 % (NSGP) 14 – 203 mmol/mol HbA1c (IFCC)			4.3 – 24.8% (NGSP) 23 to 258 mmol/mol HbA1c (IFCC)		Same
Method Comparison – Whole Blood	N=130 y-intercept = 0.2691 Slope = 1.0327 R ² =0.998			N=141 y-intercept= 0.364 Slope = 0.955 R ² =0.989		Same
Total Precision Results NGSP%	Sample	%CV		Sample	%CV	Same
	5.1%	1.6		5.25%	1.5	
	6.6%	1.3		6.63%	1.4	
	7.9%	1.3		8.11%	1.4	
	12.1%	1.1		12.09%	1.5	
Standardization	Traceable to the Diabetes Control and Complications Trial (DCCT) reference method and IFCC. Certified via the National Glycohemoglobin Standardization Program (NGSP)			Traceable to the Diabetes Control and Complications Trial (DCCT) reference method and IFCC. Certified via the National Glycohemoglobin Standardization Program (NGSP)		Same

Table 2: Differences with Predicate			
Feature	Candidate Device: VARIANT™ II TURBO HbA1c Kit – 2.0	Predicate Device: COBAS INTEGRA 800 HbA1c DX Gen. 2	Status
Hardware	VARIANT™ II TURBO Hemoglobin Testing System and VARIANT™ II TURBO Link Hemoglobin Testing System	Roche COBAS INTEGRA 800 analyzer	Technology differences do not raise new safety or efficacy concerns
Assay Principle	Ion exchange HPLC	Turbidimetric inhibition immunoassay	Technology differences do not raise new safety or efficacy concerns
Additional Matrices	Capillary blood in Hemoglobin Capillary Collection System (HCCS)	KF/Na ₂ - EDTA Na-heparin NF/K-oxalate NF/NA ₂ - EDTA Li-Heparin	Technology differences do not raise new safety or efficacy concerns

8. Summary of Performance Data:

a. Precision/Reproducibility:

The precision of the VARIANT™ II TURBO HbA1c Kit – 2.0 was evaluated based on CLSI EP05-A2 guidelines, Evaluation of Precision Performance of Quantitative Measurement Methods using a modified study design. Four EDTA whole blood samples at the following targeted HbA1c concentrations of ~5%, ~6.5%, ~8% and ~12% were utilized in the study. In addition, five quality control materials were also tested. Precision was evaluated using three reagent lots, three VARIANT™ II TURBO Hemoglobin Testing Systems at two different sites. The samples were run in duplicate in 2 runs per day for 20 days. For each sample, there were 720 measurements. Results are shown in Tables 3-6.

Table 3: Instrument 1 (% CV by Sample (NGSP))

Variation Source	Instrument ID: VART15								
	Control 1	Control 2	Patient 1	Patient 2	Patient 3	Patient 4	QC 1	QC 2	QC 3
Concentration HbA1c (NGSP%)	5.5	9.9	5.1	6.7	8.0	12.0	5.5	9.9	15.0
Repeatability	0.5%	0.3%	0.5%	0.6%	1.0%	0.3%	0.6%	0.4%	0.4%
Between-Run	0.4%	0.0%	0.3%	0.0%	0.2%	0.3%	0.3%	0.3%	0.2%
Between-Day	0.8%	0.6%	0.8%	0.7%	0.6%	0.5%	1.2%	0.8%	0.6%
Between-Lot	0.8%	0.6%	1.0%	0.8%	0.6%	0.6%	1.0%	0.5%	0.2%
Total Precision	1.4%	0.9%	1.4%	1.2%	1.3%	0.9%	1.7%	1.0%	0.8%

Table 4: Instrument 2 (% CV by Sample (NGSP))

Variation Source	Instrument ID: VART17								
	Control 1	Control 2	Patient 1	Patient 2	Patient 3	Patient 4	QC 1	QC 2	QC 3
Concentration HbA1c (NGSP%)	5.5	9.8	5.1	6.6	7.9	2.0	5.5	9.9	14.9
Repeatability	0.5%	0.3%	0.6%	0.6%	0.5%	0.4%	0.6%	0.5%	0.4%
Between-Run	0.4%	0.2%	0.5%	0.0%	0.3%	0.4%	0.0%	0.2%	0.3%
Between-Day	0.5%	0.3%	0.4%	0.5%	0.7%	0.3%	0.9%	0.7%	0.4%
Between-Lot	0.9%	0.7%	0.9%	0.7%	0.6%	0.4%	1.3%	0.6%	0.3%
Total Precision	1.2%	0.9%	1.3%	1.0%	1.1%	0.8%	1.7%	1.1%	0.8%

Table 5: Instrument 3 (% CV by Sample (NGSP))

Variation Source	Instrument ID: VartGerm01								
	Control 1	Control 2	Patient 1	Patient 2	Patient 3	Patient 4	QC 1	QC 2	QC 3
Concentration HbA1c (NGSP%)	5.4	9.7	5.1	6.6	8.0	12.1	5.4	9.8	15.0
Repeatability	0.6%	0.5%	0.8%	0.8%	0.5%	0.4%	0.8%	0.4%	0.4%
Between-Run	0.2%	0.0%	0.1%	0.0%	0.0%	0.2%	0.0%	0.2%	0.0%
Between-Day	0.6%	0.3%	0.6%	0.5%	0.5%	0.4%	0.7%	0.4%	0.3%
Between-Lot	2.0%	0.9%	1.6%	1.4%	1.0%	0.7%	2.2%	1.1%	0.7%
Total Precision	2.2%	1.1%	1.9%	1.7%	1.3%	0.9%	2.5%	1.2%	0.9%

Table 6: Instruments Combined (% CV by Sample (NGSP))

Variation Source	All Instruments								
	Control 1	Control 2	Patient 1	Patient 2	Patient 3	Patient 4	QC 1	QC 2	QC 3
Concentration HbA1c (NGSP %)	5.4	9.8	5.1	6.6	7.9	12.1	5.4	9.9	15.0
Repeatability	0.5%	0.4%	0.7%	0.7%	0.7%	0.4%	0.7%	0.5%	0.4%
Between-Run	0.3%	0.0%	0.4%	0.0%	0.2%	0.3%	0.2%	0.2%	0.2%
Between-Day	0.7%	0.4%	0.6%	0.5%	0.6%	0.4%	1.0%	0.7%	0.5%
Between-Instrument	1.3%	1.1%	0.4%	0.0%	0.4%	0.6%	0.8%	0.4%	0.0%
Between-Lot	1.4%	0.8%	1.2%	1.0%	0.8%	0.6%	1.6%	0.7%	0.5%
Total Precision	2.1%	1.5%	1.6%	1.3%	1.3%	1.1%	2.2%	1.2%	0.8%

b. Linearity

A linearity study was performed per CLSI EP06-A: Evaluation of the Linearity of Quantitative Measuring Procedures; A Statistical Approach. Linearity across the reportable range was performed using low (3.4%HbA1c) and high (20.6%HbA1c) EDTA whole blood patient samples. These samples were mixed together in varying ratios. The measured values were compared to the theoretical values based upon the dilution factor. Polynomial regression analysis (for first, second, and third order polynomials) were performed to determine the statistical significance of non-linearity. The higher order coefficients were found not to be significant and linearity was demonstrated.

% HbA1c (NGSP) using the VARIANT™ II TURBO HbA1c Kit – 2.0 has been demonstrated linear from 3.4 – 20.6% HbA1c with the maximum measured difference of $\pm 0.03\%$ between the predicted 1st and 2nd order results as shown in Table 7 below. mmol/mol HbA1c (IFCC) has been demonstrated as linear from 14 – 203 mmol/mol with the maximum measured difference of $\pm 0.3\%$ (or +/- 0.38mmol/mol) as shown in Table 8 below.

Table 7: Results of Linearity Study (NGSP %)

Sample Pool	Predicted 1st Order	Predicted 2nd Order	Difference
Level 1	3.39	3.41	-0.03
Level 2	5.12	5.13	-0.01
Level 3	6.85	6.85	0.00
Level 4	8.58	8.57	0.01
Level 5	10.31	10.29	0.01
Level 6	12.04	12.02	0.01
Level 7	13.77	13.75	0.01
Level 8	15.50	15.49	0.01
Level 9	17.23	17.23	0.00
Level 10	18.96	18.98	-0.02
Level 11	20.69	20.72	-0.03

Table 8: Results of Linearity Study (IFCC mmol/mol)

Sample Pool	Predicted 1st Order	Predicted 2nd Order	Difference
Level 1	14	14	-0.32
Level 2	32	33	-0.14
Level 3	51	51	-0.01
Level 4	70	70	0.09
Level 5	89	89	0.15
Level 6	108	108	0.16
Level 7	127	127	0.13
Level 8	146	146	0.07
Level 9	165	165	-0.04
Level 10	184	184	-0.19
Level 11	203	203	-0.38

c. Method Comparison

A Method comparison study was performed per CLSI EP09-A2 IR, Method Comparison and Bias Estimation Using Patient Samples. 130 variant-free whole blood EDTA samples ranging from 3.4% to 20.0% HbA1c were evaluated using the VARIANT™ II TURBO HbA1c Kit- 2.0 on the VARIANT™ II TURBO Hemoglobin Testing System. Samples were tested in a single determination over a 4 day period. The results were compared to testing performed at a secondary NGSP SRL reference laboratory using a

cleared HPLC-based HbA1c assay. The distribution of samples spanned the measuring interval listed in Table 9.

Table 9: Distribution of samples

Hemoglobin A1c level	n	% Samples tested
≤ 5%	6	4.6
5 – 6%	17	13.1
6 – 6.5%	33	25.4
6.5 – 7%	31	23.8
7 – 8%	21	16.2
8 – 9%	11	8.5
> 9%	11	8.5
Total samples	130	100

Deming (weighted) and Passing-Bablok regression analyses were performed for the VARIANT™ II TURBO HbA1c Kit – 2.0 versus the NGSP SRL reference method.

Table 10: Summary of Method Comparison Results

	y-Intercept	95% CI	Slope	95% CI
Deming	-0.275	-0.342 – 0.208	1.033	1.023 – 1.043
Passing-Bablok	-0.331	-0.419 – 0.255	1.041	1.029 – 1.054

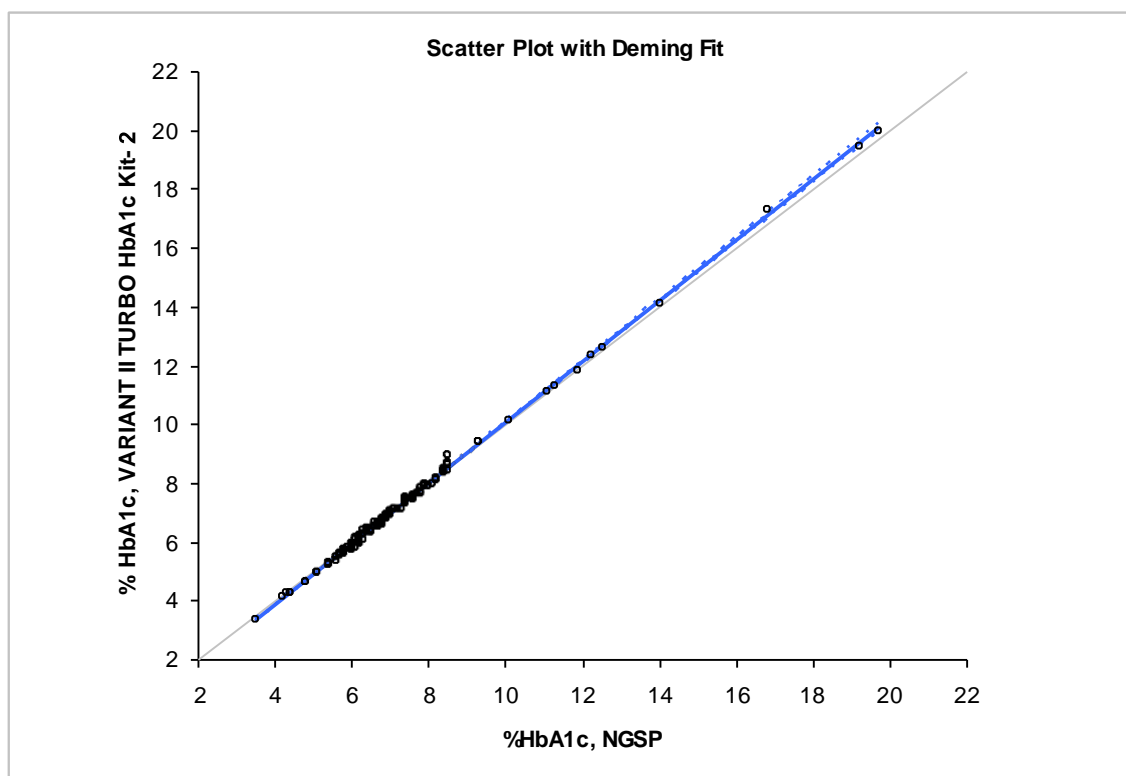


Figure 1: Scatter Plot using Deming Fit, %HbA1c, NGSP SRL vs. VARIANT™ II TURBO HbA1c Kit – 2.0

The following biases between VARIANT™ II TURBO HbA1c Kit – 2.0 versus NGSP SRL Method (Reference method) were observed:

Table 11: Bias Estimation

% HbA1c – Decision Level	Bias	% Bias
5.0	-0.11	-2.11
6.5	-0.06	-0.87
8.0	-0.01	-0.09
12.0	0.12	1.03

Total Error Decision Levels

Using the results of bias estimation (%Bias) in the method comparison study and precision estimates in the reproducibility study, Total Error (TE) at four concentrations: (5.0 %, 6.5%, 8.0% and 12.0%) were calculated as follows: $\%TE = |\%Bias| + 1.96 * CV * (1 + \%Bias)$. The results are presented in the Table 12.

Table 12: Total Error Estimation

% A1c – Decision Level	% Bias	% CV	% TE
5.0	-2.11	1.6	5.2
6.5	-0.87	1.3	3.4
8.0	-0.09	1.3	2.6
12.0	1.03	1.1	3.2

d. Traceability, Stability, Expected Values (calibrators)

The assigned HbA1c values of the VARIANT™ II TURBO HbA1c Kit -2.0 are certified with the National Glycohemoglobin Standardization Program (NGSP). The final reportable result is traceable to both the International Federation of Clinical Chemistry (IFCC) and the Diabetes Control and Complications Trial (DCCT). The International Federation of Clinical Chemistry (IFCC) units of mmol/mol are calculated using the Master Equation NGSP (%) = $0.09148 \times \text{IFCC (mmol/mol)} + 2.152$. HbA1c results are provided to the customers using two different units: NGSP equivalent units (%) and IFCC equivalent units (mmol/mol).

Calibrator Materials:

Value assignment for calibrators (VARIANT™ II TURBO HbA1c Kit – 2.0 Calibrator/Diluent Set) which are recommended for use with this device, were previously reviewed under 510(k) submission K070452.

e. Analytical specificity:

i.) Endogenous Interference

An Endogenous Interference study was performed per CLSI EP07-A2, Interference Testing in Clinical Chemistry. Two EDTA whole blood sample pools were evaluated using a low level whole blood sample with a concentration ~6.5% HbA1c and a high level whole blood sample with a concentration of HbA1c of ~8.0%.

Conjugated bilirubin, unconjugated bilirubin and glucose, available in pure form, were obtained and stock solutions prepared at 10x the intended test

concentration. The 10x stock solution of the test substance was pipetted into a low whole blood sample pool (at ~6.5% HbA1c) and a high whole blood sample pool (~8.0% HbA1c), making the test pool. Ten replicates of each pool prepared with the test and control samples were analyzed using the VARIANT™ II TURBO HbA1c Kit-2.0 on the VARIANT™ II TURBO Hemoglobin Testing System.

Rheumatoid factor, lipemia and total protein were not available as pure standards therefore serum samples with known concentration of these compounds were used. The test pool was prepared by mixing the serum sample known to have a high test substance concentration with a whole blood non-variant sample such that the concentration of test substance in the final mixture would be at the desired level. Ten replicates of each pool prepared with the test and control samples were analyzed using the VARIANT™ II TURBO HbA1c Kit-2.0 on the VARIANT™ II TURBO Hemoglobin Testing System.

Significant interference was defined as a $\pm 7\%$ change in %HbA1c value from the control. Results in Table 13 showed no significant interference up to the stated concentrations.

Table 13: Endogenous Interference Study Results

Endogenous substance	Concentration	
	Conventional (US) units	SI Units
Lipemia (Intralipid)	6000 mg/dL	60 g/L
Conjugated bilirubin	60 mg/dL	712 μ mol/L
Unconjugated bilirubin	60 mg/dL	1026 μ mol/L
Glucose	2000 mg/dL	111 mmol/L
Rheumatoid factor	750 IU/mL	750 kIU/mL
Total protein	21 g/dL	210 g/L

ii.) Drug Interference:

A Drug Interference study was performed based per CLSI EP07-A2, Interference Testing in Clinical Chemistry. Two EDTA whole blood sample pools were evaluated using a low level whole blood sample with a concentration ~6.5%HbA1c and a high level whole blood sample with a concentration of ~8.0%HbA1c. Test samples were prepared by spiking each drug at the interferent concentration shown in Table 14. Ten replicates of each drug prepared with the test and control samples were analyzed using the VARIANT™ II TURBO HbA1c Kit-2.0 on the VARIANT™ II TURBO Hemoglobin Testing System.

Significant interference was defined as a more than $\pm 7\%$ change in %HbA1c value from the control. No significant interference was observed at therapeutic levels up to the stated concentrations in Table 14.

Table 14: Drug Interference Study Results

Potential Drug Interferent	Highest Level Tested showing no Significant Interference	
	Conventional (US) units	SI units
Acetylcysteine	166 mg/dL	10.2 mmol/L
Ampicillin-Na	1000 mg/dL	28.65 mmol/L
Ascorbic acid	300 mg/dL	17.05 mmol/L
Cefoxitin	2500 mg/dL	58.55 mmol/L
Heparin	5000 U/L	5000 U/L
Levodopa	20 mg/dL	1015 µmol/L
Methyldopa	20 mg/dL	948 µmol/L
Metronidazole	200 mg/dL	11.7 mmol/L
Doxycyclin	50 mg/dL	1124 µmol/L
Acetylsalicylic acid	1000 mg/dL	55.51 mmol/L
Rifampicin	64 mg/L	78 µmol/L
Cyclosporine	5 mg/L	4 µmol/L
Acetaminophen	200 mg/L	1323 µmol/L
Ibuprofen	500 mg/L	2427 µmol/L
Theophylline	100 mg/L	556 µmol/L
Phenylbutazone	400 mg/L	1299 µmol/L

iii.) Cross Reactivity with Hemoglobin Derivatives:

A Hemoglobin Derivatives Interference study was performed based on CLSI EP07-A2, Interference Testing in Clinical Chemistry. Potential interference from Acetylated hemoglobin (Hb), Carbamylated hemoglobin (Hb) and Labile HbA1c were evaluated using a low level whole blood EDTA sample with a concentration ~6.5% HbA1c and a high level whole blood EDTA sample with a concentration of ~8.0% HbA1c. The potentially interfering hemoglobin derivatives were spiked into the low and high level blood samples and each sample was analyzed using ten replicates each in the same analytical run on the VARIANT™ II TURBO Hemoglobin Testing System with the VARIANT™ II TURBO HbA1c Kit – 2.0.

Significant interference was defined as more than a $\pm 7\%$ change in HbA1c value from the control. The test result conclusions are as follows:

- Acetylated Hb- up to 50 mg/dL does not interfere with this assay.
- Carbamylated Hb – up to 4% (2.6 mM potassium cyanate) does not interfere with this assay.
- Labile A1c- up to 6% (1000mg/dL) glucose does not interfere with this assay.

Results showed there was no cross reactivity with these substances at physiological levels.

iv.) Hemoglobin Variant Study:

A Hemoglobin Variant study was performed using specific variant samples known to contain hemoglobin variants S, C, E, D, A2 and F. Two whole blood EDTA patient samples containing an HbA1c $\sim 6.5\%$ and $\sim 8\%$ and the appropriate hemoglobin variant were tested. Testing of the samples containing hemoglobin variants S, C, E, D, A2 and F were performed in duplicate. Testing of the samples was performed using the VARIANT™ II TURBO HbA1c Kit – 2.0 on the VARIANT™ II TURBO Hemoglobin Testing System and compared to results obtained by a NGSP reference method that has been demonstrated to be free from the hemoglobin interferent. Table 15 contains the number of samples, range of samples and concentration of samples used in the Hemoglobin Variant Study. Table 16 contains the results for the Hemoglobin Variant study bias.

Table 15: Variant samples used in Hemoglobin Variant Study

Hemoglobin Variant	n	Range in % Abnormal Variant	Range in %HbA1c Concentration
HbS	26	26.8 – 41.6	6.0 – 8.6
HbC	25	33.3 – 42.4	6.1 – 7.9
HbD	21	30.2 – 41.9	6.1 – 8.6
HbE	24	24.7 – 31.4	6.1 – 8.3
HbA2	22	5.0 – 10.2	5.4 – 14.5
HbF	29	3.5 – 29.2	5.4 – 14.4

Table 16: Hemoglobin Variant Study Bias Results

Hemoglobin Variant	Relative % Bias from Reference Method observed at Low and High Concentrations of HbA1c	
	Relative % Bias (StDev) for HbA1c $\sim 6.5\%$	Relative % Bias (StDev) for HbA1c $\sim 8.0\%$
HbS	1.9 (± 2.8)	2.8 (± 1.8)
HbC	-0.3 (± 3.5)	-2.5 (± 2.5)
HbD	-1.1 (± 1.7)	-1.2 (± 1.0)
HbE	0.7 (± 3.0)	2.2 (± 1.4)
HbF	-1.9 (± 3.1)	-0.1 (± 2.1)
HbA2	1.4 (± 2.3)	2.0 (± 4.1)

2. Matrix comparison

The data supports the use of the following blood collection tubes and collection system with the VARIANT™ II TURBO HbA1c Kit – 2.0.

- K₂-EDTA
- K₃-EDTA
- Hemoglobin Capillary Collection System (HCCS).

3. Expected Values/Reference Range

Hemoglobin A1c expected values range was cited from American Diabetes Association Standards of Medical Care in Diabetes 2010, 33 (Supplement 1), S62-S69 for Diagnosis of Diabetes.

Table 17: Hemoglobin A1c Expected Values

Hemoglobin A1c		Suggested Diagnosis
NGSP %	IFCC mmol/mol	
>6.5	>47	Diabetic
5.7 – 6.4	39-46	Pre-Diabetic
<5.7	<39	Non-Diabetic

4. Satisfaction of Special Controls Requirements for Diabetes Diagnosis Claim

VARIANT™ II TURBO/TURBO Link
Status of Special Controls for HbA1c for Diabetes Diagnosis

Yes/No	Requirement
YES	Device must have initial and annual standardization verification by a certifying glycohemoglobin standardization organization deemed acceptable by the FDA.
YES	Performance testing of device precision must, at a minimum, use blood samples with concentrations near 5.0%, 6.5%, 8.0% and 12% hemoglobin A1c. Testing must evaluate precision over a minimum of 20 days using at least 3 lots of the device and 3 instruments, as applicable.
YES	Performance testing of accuracy must include a minimum of 120 blood samples that span the measuring interval of the new device and compare results of the new device to results of the standardized method. Results must demonstrate little or no bias versus the standardized method.
YES	Total error of the new device must be evaluated using single measurements by the new device compared to results of the standardized test method, and this evaluation must demonstrate a total error less than or equal to 6%.
YES	Performance testing must demonstrate that there is little to no interference from common hemoglobin variants, including Hemoglobin C, Hemoglobin D, Hemoglobin E, Hemoglobin A2 and Hemoglobin S.
N/A	When assay interference from Hemoglobin F or interference with other hemoglobin variants with low frequency in the population is observed, a warning statement must be placed in a black box and must appear in all labeling material for these devices describing the interference and any affected population.

Conclusion:

The information and data in this 510(k) document demonstrate that the VARIANT™ II TURBO HbA1c Kit – 2.0 as performed on the VARIANT™ II TURBO and VARIANT™ II TURBO Link Hemoglobin Testing Systems is an accurate, reliable, precise test that correlates well with current cleared methods and NGSP standardized testing for the quantitation of HbA1c. The contents of this submission demonstrates that the VARIANT™ II TURBO HbA1c Kit – 2.0 as performed on the VARIANT™ II TURBO and VARIANT™ II TURBO Link Hemoglobin Testing Systems is substantially equivalent to its predicate device, Cobas Integra 800 Tina-quant HbA1cDX Gen. 2 Assay and, therefore, safe and effective for its intended use. The performance criteria as stipulated by the Special Controls requirements for HbA1c systems that diagnose diabetes have clearly been met. The VARIANT™ II TURBO HbA1c Kit – 2.0 must be found to be substantially equivalent to the predicate and, therefore, cleared by the agency for the intended use requested.